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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,446	09/13/2004	Hidetsugu Goto	4439-4024	8215

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MORGAN & FINNEGAN, L.L.P.
3 WORLD FINANCIAL CENTER
NEW YORK, NY 10281-2101

EXAMINER	
GANGLE, BRIAN J	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/507,446	GOTO ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *1, 4-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/13/04;3/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II in the reply filed on 9/15/2006 is acknowledged. The traversal is on the ground(s) that the inventions have not been shown to be independent or distinct, and no search burden has been shown. This is not found persuasive because independence or distinctness and search burden are not criteria in determining whether a restriction is proper when said restriction is made under PCT Rules 13.1 and 13.2.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10 are pending. Claims 1 and 4-9 are withdrawn as being drawn to non-elected inventions. Claims 2, 3, and 10 are currently under examination.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 9/13/2004 and 3/10/2006 have been considered. Initialed copies are enclosed.

Claim Objections

Claims 3 and 10 are objected to because of the following informalities: the claims are drawn, in part, to non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2 and 3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claimed invention is drawn to a product of nature. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. The claimed DNA molecule can be found naturally in *Gluconacetobacter*.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The instant claims are drawn to a DNA of a gene encoding an SPT protein that is (A) a protein having an amino acid sequence shown in SEQ ID NO:2; or (B) a protein consisting of an amino acid sequence comprising substitution, deletion, insertion, addition, or inversion of one or several amino acids in an amino acid sequence shown in SEQ ID NO:2 and having a function of enhancing acetic acid tolerance. As drawn, the claim encompasses practically any piece of DNA. A single nucleotide would meet the limitations of the claims, so long as that nucleotide can be found in SEQ ID NO:2. Further, the nucleotide can also be from a protein that has *a* sequence shown in SEQ ID NO:2 (meaning any sequence found within SEQ ID NO:2), and that sequence can have substitutions, deletions, insertions, additions, or inversions, so long as the protein has the function of enhancing acetic acid tolerance.

This claim encompasses a vast genus of polynucleotides that have no correlation between their structure and function (i.e. enhancing acetic acid tolerance). None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that

"applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of

the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:1 and 2, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid and/or protein itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2datl966.

Therefore, only SEQ ID NO:1 and 2, but not the full breadth of the claims, meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115).

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA with the sequence of SEQ ID NO:1, or encoding the protein

with the amino acid sequence of SEQ ID NO:2, does not reasonably provide enablement for the multitude of nucleic acids claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claim encompasses any DNA of a gene encoding an SPT protein that is (A) a protein having an amino acid sequence shown in SEQ ID NO:2; or (B) a protein consisting of an amino acid sequence comprising substitution, deletion, insertion, addition, or inversion of one or several amino acids in an amino acid sequence shown in SEQ ID NO:2 and having a function of enhancing acetic acid tolerance. As drawn, the claim encompasses practically any piece of DNA. A single nucleotide would meet the limitations of the claims, so long as that nucleotide can be found in SEQ ID NO:2. Further, the nucleotide can also be from a protein that has *a* sequence shown in SEQ ID NO:2 (meaning any sequence found within SEQ ID NO:2), and that sequence can have substitutions, deletions, insertions, additions, or inversions, so long as the protein has the function of enhancing acetic acid tolerance. The claim encompasses a vast genus of polypeptides that have no correlation between their structure and function. The specification does not disclose which portions of SEQ ID NO:2 are necessary to provide the claimed function (i.e. enhancing acetic acid tolerance). Protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). The sensitivity of proteins to alterations of even a single

amino acid in a sequence are exemplified by Burgess et al (J. of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al. (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Clearly, variants or fragments of SEQ ID NO:2 that maintained the characteristics of the SEQ ID NO:2 could not be predicted, and there is no way to predict what specific immune response would be elicited. Additionally, Bork (Genome Research, 2000,10:398-400) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, column 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, column 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, column 3). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, column 2). Most features predicted with an accuracy of greater than 70% are of structural nature and, at best, only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399, paragraph bridging columns 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those features are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, paragraph bridging cols 1 and 2). Clearly, given not only the teachings of Bowie et al., Lazar et al. and Burgess et al. but also the limitations and pitfalls of using computational

sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function as taught by Bork, the claimed proteins could not be predicted based on sequence identity to SEQ ID NO:2. Clearly, it could not be predicted that polypeptide or a variant that shares only partial homology with a disclosed protein or that a protein that is encoded by a "variant" of a given SEQ ID NO. will function in a given manner (i.e. enhancing acetic acid tolerance). Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use the claimed genus of proteins. In view of the above, with the exception of SEQ ID NO:1 and 2, one of skill in the art would be forced into undue experimentation to practice the full scope of the claimed invention.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the plasmid represented by the accession number, FERM BP-7932 and the designation pUSPT, is required in order to practice the invention. Specifically, it is noted that claim 10 recites deposited material. The deposit of biological organisms is considered by the Examiner to be necessary for the enablement of the current invention (see 37 CRF 1.808(a)). The examiner acknowledges the deposit of organisms under the accession number FERM BP-7932 in partial compliance with this requirement. However, said deposits are not in full compliance with 37 CFR 1.803-1.809.

If the deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit, or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a

position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the following criteria have been met:

1) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

2) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent; and

3) the deposits will be maintained for a term of at least thirty (30) years from the date of the deposit or for the enforceable life of the patent or for a period of at least five (5) years after the most recent request for the furnishing of a sample of the deposited material, whichever is longest; and

4) a viability statement in accordance with the provisions of 37 CFR 1.807; and

5) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CRF 1.809(d) should be added to the specification. See 37 CFR 1.803 - 1.809 for additional explanation of these requirements.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 3 are rendered vague and indefinite by the phrase "DNA of a gene encoding the protein SPT." Genes are composed of DNA. Are applicants simply claiming DNA that encodes the protein SPT? Is there a difference between DNA that encodes a protein and DNA of a gene that encodes a protein?

Claim 3 is rendered vague and indefinite by the phrase "DNA that comprises a nucleotide sequence consisting of nucleotides 187 to 1386 shown in SEQ ID NO:1 in the sequence listing

within the nucleotide sequence." It is not clear what the last phrase, "within the nucleotide sequence" is referring to or why it is in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by the Stratagene catalog (Stratagene Cloning Systems, 1993).

The instant claim is drawn to a DNA of a gene encoding the protein SPT described in following (A) or (B): (A) A protein having an amino acid sequence shown in SEQ. ID NO:2 in the sequence listing. (B) A protein consisting of an amino acid sequence comprising substitution, deletion, insertion, addition, or inversion of one or several amino acids in an amino acid sequence shown in SEQ. ID NO:2 in the sequence listing and having a function of enhancing acetic acid tolerance.

The Stratagene catalog discloses a deoxynucleotide mix that contains the four nucleotides, each of which is *a* DNA from a gene encoding a protein having an amino acid sequence shown in SEQ ID NO:2 (see page 88).

Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by the Invitrogen catalog (Invitrogen, 2001).

The instant claim is drawn to a DNA of a gene encoding the protein SPT described in following (A) or (B): (A) A protein having an amino acid sequence shown in SEQ ID NO:2 in the sequence listing. (B) A protein consisting of an amino acid sequence comprising substitution, deletion, insertion, addition, or inversion of one or several amino acids in an amino acid sequence shown in SEQ. ID NO:2 in the sequence listing and having a function of enhancing acetic acid tolerance.

The Invitrogen catalog discloses a random primer set that contains every possible hexameric DNA sequence (page 35). This would necessarily include a sequence of DNA that would come from a gene encoding a protein having an amino acid sequence shown in SEQ ID NO:2..

Conclusion

No claim is allowed.

SEQ ID NO:1 and 2 are free of the art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brian Gangle
AU 1645

ROBERT A. ZEMAN
PRIMARY EXAMINER